

# Congenital Toxoplasmosis in a 6-week-old Boy, Presenting with Fever and Right Leg Monoplegia

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## Abstract

We report a 6-week-old boy presenting with fever, unable to move right leg, abdominal distension, swelling of right testis and oliguria for 1 day. He was born as a 32-week preterm infant with birth weight of 1,720 g. Prenatal VDRL, anti-HIV and HBsAg were negative. Physical examination revealed body weight of 2,050 g, body temperature of 38°C, alert, anterior fontanel 3 × 3 cm, hepatosplenomegaly, hypospadias, swelling of right testis, bilateral motor weakness (more prominent on right side) and hyporeflexia. Laboratory results: Hct 28 percent, wbc 17,000 cells/mm<sup>3</sup>, platelet 229,000/mm<sup>3</sup>; x-ray of right femur and spine were normal; cerebrospinal fluid: wbc 37 cells/mm<sup>3</sup> (all lymphocyte). He was treated as orchitis with cefotaxime 100 mg/kg/day. During hospitalization, he developed generalized tonic clonic seizure. Computerized tomogram of the brain revealed generalized intracranial calcification and hydrocephalus. Eye examination showed chorioretinitis. Anti-toxoplasmosis IgG, IgM of the patient and his mother were positive. Diagnosis of congenital toxoplasmosis was made and treatment was started with sulfadiazine, pyrimethamine, leucovorin and prednisolone. He developed hepatitis from sulfadiazine and antibiotic was changed to clindamycin. The defervescence was noticed on the 5<sup>th</sup> day of treatment. Ventriculoperitoneal shunt was performed. Seizure was controlled with phenobarbital and prednisolone was discontinued within one month. The plan for the total course of treatment is one year. At the present time, he has received treatment for 10 months and overall clinical symptoms were improved, with delayed development, spasticity of right leg and blindness. Although congenital toxoplasmosis was uncommon, appropriate treatment will improve clinical symptoms. Delayed diagnosis and treatment result in a poor prognosis. Education, prenatal and neonatal screening seem to be good strategies to prevent congenital toxoplasmosis and give early treatment. However, the cost benefit of screening should be studied. (*J Infect Dis Antimicrob Agents* 2000;18:24-7.)

## INTRODUCTION

Congenital toxoplasmosis is an uncommon but treatable disease. The patients may present with various symptoms with involvement of central nervous system (CNS), ocular system, and reticuloendothelial

system. We report a case of congenital toxoplasmosis with uncommon CNS presentation. High index of suspicion and awareness of the disease are important for making diagnosis and lead to appropriate treatment.

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## CASE REPORT

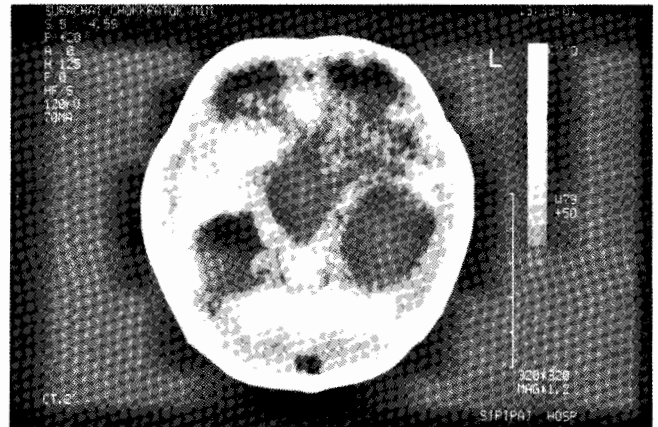
A 6-week-old male infant presented with fever, inability to move right leg, and scrotal swelling. He was born to a 20-year-old mother with negative hepatitis B surface antigen, Venereal Disease Research Laboratory (VDRL) test, and anti-HIV antibody at 32 weeks gestation age and 3 days after membrane rupture with chorioamnionitis. His birth weight was 1,720 g and the apgar score was 8 and 9 at 1<sup>st</sup> and 5<sup>th</sup> minute, respectively. Physical examination at birth was normal except for hypospadias and undescended left testis. He was put on penicillin and gentamicin for 7 days for the treatment of chorioamnionitis and went home after 20 days of admission. He had appropriate weight gain with breast feeding and infant formula. At one month of age, he received BCG and hepatitis B vaccination. He was able to smile.

One week prior to this admission, he developed abdominal distension. One day before admission, he developed fever, swelling of right testis, decreased urination, and stopped moving his right leg. There was no history of trauma. Physical examination revealed body weight of 2,050 g, length of 48 cm, head circumference of 34.5 cm (40<sup>th</sup>, 10<sup>th</sup>, and 80<sup>th</sup> percentile respectively after correction for gestational age), body temperature of 38°C, respiratory rate of 40/min, heart rate of 142/min and blood pressure of 88/55 mmHg. His anterior fontanelle was 3 × 3 cm without bulging, and posterior fontanelle was 1 × 1 cm. He had hepatosplenomegaly, hypospadias, undescended left testis, and swelling and erythema of right testis with positive transillumination test.

Neurological examination revealed an alert infant with flaccid paralysis, hypotonia and hyporeflexia of right leg. Motor power of the left leg was decreased to grade III/IV. He had uncontrolled urinary dripping. Sensation was normal. No other neurological deficit was detected. The initial laboratory tests revealed hemoglobin of 9.5 g/dl, hematocrit of 28 percent, white blood count of 17,000/mm<sup>3</sup> (21% polymorphonuclear cells, 53% lymphocytes, 12% eosinophil, 2% monocyte, 1% basophil, and 11% large unstained cell), and platelet count of 229,000/mm<sup>3</sup>. The urine analysis, stool examination, blood chemistry, as well as the roentgenogram of hips, spines and chest were normal. Cerebrospinal fluid (CSF) analysis revealed 37 white blood cell (100% lymphocytes), 27 fresh red blood cells, protein of 79 mg/dl, CSF: blood sugar ratio of 25:102 mg/dl,

and no organism identified by gram staining. The CSF was sent for enterovirus, poliovirus, adenovirus, herpes simplex virus and cytomegalovirus (CMV) cultures, and stool was sent for enterovirus and poliovirus cultures.

His right testis became normal after cefotaxime therapy. On the 5<sup>th</sup> day of admission, he developed subtle seizure. Computerized tomogram (CT) of the brain revealed communicating hydrocephalus with generalized calcification (Figure 1). The eye examination revealed chorioretinitis involving posterior pole with vitreous reaction in both eyes. The hearing test was normal. The serology confirmed the diagnosis of congenital toxoplasmosis by positive anti-toxoplasma IgG and IgM in both the infant and his mother. The CSF viral cultures were negative. The serology for other congenital infections were negative except for anti-CMV which was positive for IgG but negative for IgM.



**Figure 1. CT scan of brain demonstrating communicating hydrocephalus with scattered intracranial calcification.**

He was put on sulfadiazine 100 mg/kg/day, pyrimethamine 2 mg/kg for 2 days then 1 mg/kg/day, leucovorin 5 mg/kg/day, and prednisolone 2 mg/kg/day. He was afebrile after 5 days of treatment. Ventriculoperitoneal shunt was placed. Prednisolone was tapered after 1 month when the repeated eye examination revealed improvement with residual macular scar. He developed hepatitis from sulfadiazine which was subsided after changing to clindamycin. The convulsion was controlled by phenobarbital and neurogenic bladder was improved. He was able to urinate completely after 2 months of treatment. He developed spasticity with hyperreflexia of right leg. At 7 months of age, he was active, with improved motor function

of both legs. He was, however, blind.

## DISCUSSION

Infants who appear normal at birth and present with hepatosplenomegaly and neurological deficit within a few months of life remind pediatricians to be aware of perinatally acquired infections including CMV, toxoplasmosis, syphilis, herpes simplex virus, tuberculosis, and human immunodeficiency virus (HIV). Acute onset of fever and neurological deficit particularly with abnormal CSF findings and convulsion suggest acute CNS infections. Viral meningoencephalitis may cause focal motor deficit and neurogenic bladder similar to this infant. The common etiologic agents of meningoencephalitis including enteroviruses, adenovirus, herpes simplex virus were investigated in our patient.

We were able to make the diagnosis in this infant by CT scan and serology. The typical scattered calcification pattern is pathognomonic for congenital toxoplasmosis. This patient manifested the extreme level of CNS involvement including cerebral damage and hydrocephalus. Only 10 percent of congenital toxoplasmosis presents in this level of severity.<sup>1</sup> Chorioretinitis has been commonly found and may cause blindness which was found in our patient. Although *Toxoplasma* can be inhibited or killed by medical therapy, the damaged organs may not recover. Early diagnosis and prompt treatment help preserve the organs that has not yet damaged and stop the progression of disease.

Infants and children have regenerative potentials and may overcome the damaged parts. Efficacy of medical treatment has been proven in many studies to help improve the outcomes.<sup>2,3</sup> Pyrimethamine plus sulfadiazine has been currently known as the effective standard regimen. Clindamycin and new macrolides such as clarithromycin and azithromycin are also effective and are alternative drugs for patients who cannot tolerate the standard regimen. Leucovorin should be used to reduce bone marrow toxicity of pyrimethamine. Corticosteroid stops the progression of chorioretinitis as well as leptomenigeal inflammation which results in hydrocephalus and should be used in the initial stage of treatment. Treatment must be continued for at least 1 year.

The clinicians should diagnose congenital toxoplasmosis before the occurrence of damage. Most cases of congenital toxoplasmosis were asymptomatic

or subclinical infection. However, it may result in long term neurological sequelae such as mental retardation, seizure, late onset chorioretinitis, and hearing loss.<sup>4,5</sup> If diagnosis can be established in these asymptomatic cases before any insult occurred, the treatment outcome is excellent. Congenital toxoplasmosis in healthy population occurs only in the setting of maternal primary infection during pregnancy. Therefore, in order to diagnose and treat all cases of congenital toxoplasmosis, regardless of symptoms in infants, prenatal screening and treatment in susceptible pregnant women who seroconverted during pregnancy was studied.<sup>6-9</sup> Further investigations to diagnose fetal infection were performed among these women. If fetal infection was detected, treatment regimen in the mother was then changed from spiramycin to pyrimethamine plus sulfadiazine after the first trimester. Treatment in infected women helps reduce rate and severity of fetal infection.<sup>8</sup> With this prenatal screening and treatment program in French and Austria<sup>6,7</sup>, the incidence of congenital toxoplasmosis decreased significantly. The European Research Network on Congenital Toxoplasmosis initiated this program in 5 European university medical centers in 1993 and found reduction of mother to infant transmission by prenatal treatment from 72 to 39 percent.<sup>8</sup> The study in Finland found the annual cost of congenital toxoplasmosis reduced from 128 to 98 US dollars per pregnancy with prenatal screening.<sup>9</sup> The strategy of prenatal screening requires comprehensive obstetrical care that may not be feasible in developing countries. Another strategy to detect asymptomatic congenital toxoplasmosis is neonatal screening by detecting anti-toxoplasma IgM from dry blood spot that is available in many countries for neonatal metabolic screening.<sup>10-12</sup> The problem is the false positive and false negative tests particularly in countries with low incidence of the disease. Moreover, the cost of the test is high.<sup>12</sup> The cost benefit of this strategy in each country needs to be determined. In Thailand, the prevalence of congenital toxoplasmosis is not known. The data from previous studies revealed seroprevalence of 13-21 percent among pregnant women<sup>13,14</sup>, but most of these seropositives had negative IgM indicating remote infections. There has been no study on the rate of acquisition of infection during pregnancy. However, the cases of symptomatic congenital toxoplasmosis have been

rarely reported.

The basic strategy to prevent congenital toxoplasmosis is to prevent infection during pregnancy. Pregnant women should be routinely instructed to avoid eating or handling raw or uncooked meat as well as good hygienic practice when handling cat, cat's feces, fresh fruits and vegetables, and gardening.

Finally, clinicians should be alert for congenital toxoplasmosis that may present with various complaints and try to make diagnosis as early as possible. Serology particularly anti-toxoplasma IgM is helpful but can be negative in many cases of congenital toxoplasmosis or may be false positive. Treatment should be implemented in any cases with high clinical suspicion, even with negative anti-toxoplasma IgM. These infants usually develop IgM later, sometimes at the end of the first year. Therefore, repeated serological studies is needed. In patients with positive IgM without evidence of maternal infection, false positive results may be possible, and repeating the test is necessary.

In conclusion, congenital toxoplasmosis is an uncommon but treatable congenital infection. High index of suspicion is needed to make early diagnosis. Delayed diagnosis and treatment result in poor outcome. Strategies such as prenatal and neonatal screening to diagnose this infection which may be subclinical and offer the treatment can prevent the long term sequelae. However, cost benefit of these strategies should be studied in each country.

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